



## HESX1 gene

HESX homeobox 1

### Normal Function

The *HESX1* gene provides instructions for producing a protein that regulates the activity of other genes. On the basis of this action, the HESX1 protein is called a transcription factor. The *HESX1* gene is part of a family of homeobox genes, which act during early embryonic development to control the formation of many body structures.

The HESX1 protein plays an important role in early brain development. In particular, it is essential for the formation of the pituitary, which is a gland at the base of the brain that produces several hormones. The HESX1 protein is also necessary for the development of structures at the front of the brain (the forebrain), including the nerves that carry visual information from the eyes to the brain (optic nerves).

The HESX1 protein interacts with other proteins, including the protein produced from the *PROP1* gene, during embryonic development. Both the HESX1 protein and the PROP1 protein bind to DNA and control the activity of other genes. The HESX1 protein turns off (represses) genes, while the PROP1 protein turns on (activates) genes. These proteins work together to coordinate the development of certain parts of the brain.

### Health Conditions Related to Genetic Changes

combined pituitary hormone deficiency

septo-optic dysplasia

At least five mutations in the *HESX1* gene have been identified in people with septo-optic dysplasia. Some of these mutations change single DNA building blocks (base pairs) in the *HESX1* gene, while others insert or delete genetic material in the gene. Mutations in this gene alter the function of the HESX1 protein, for example by preventing it from binding to DNA and repressing the activity of other genes. *HESX1* gene mutations disrupt the formation and early development of the pituitary gland, optic nerves, and other brain structures. These abnormalities of brain development lead to the characteristic features of septo-optic dysplasia.

Studies suggest that mutations in the *HESX1* gene are a rare cause of septo-optic dysplasia.

### other disorders

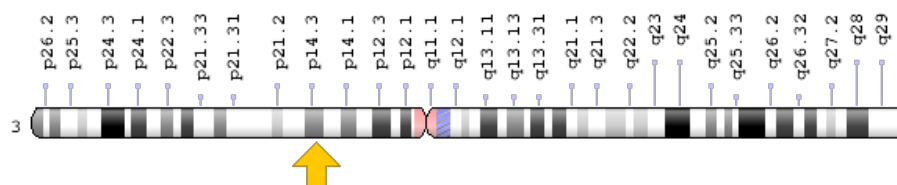
More than a dozen *HESX1* gene mutations have been found to cause underdevelopment (hypoplasia) of the pituitary gland in people without the other characteristic features of septo-optic dysplasia. Pituitary hypoplasia leads to a shortage of hormones needed for growth, reproduction, and other critical body functions. Affected individuals may also have signs and symptoms affecting other parts of the body, including genital abnormalities, vision impairment, distinctive facial features, and extra (supernumerary) fingers.

Mutations in the *HESX1* gene lead to the production of a defective or nonfunctional HESX1 protein, which disrupts the formation of the pituitary gland during critical stages of embryonic development. Some mutations prevent the HESX1 protein from binding to DNA and repressing the activity of other genes. Other mutations prevent the HESX1 protein from interacting with the PROP1 protein to coordinate brain development. It is unclear how mutations in the *HESX1* gene can cause signs and symptoms affecting other parts of the body.

### **Chromosomal Location**

Cytogenetic Location: 3p14.3, which is the short (p) arm of chromosome 3 at position 14.3

Molecular Location: base pairs 57,197,838 to 57,227,643 on chromosome 3 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

### **Other Names for This Gene**

- ANF
- CPHD5
- HESX1\_HUMAN
- homeobox, ES cell expressed 1
- Rathke pouch homeobox
- RPX

## **Additional Information & Resources**

### Educational Resources

- Endocrinology: An Integrated Approach (first edition, 2001): The Pituitary Gland  
<https://www.ncbi.nlm.nih.gov/books/NBK27/>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28HESX1%5BTIAB%5D%29+OR+%28RPX%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

### OMIM

- HOMEBOX GENE EXPRESSED IN ES CELLS  
<http://omim.org/entry/601802>

### Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
[http://atlasgeneticsoncology.org/Genes/GC\\_HESX1.html](http://atlasgeneticsoncology.org/Genes/GC_HESX1.html)
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=HESX1%5Bgene%5D>
- HGNC Gene Family: PRD class homeoboxes and pseudogenes  
<http://www.genenames.org/cgi-bin/genefamilies/set/521>
- HGNC Gene Symbol Report  
[http://www.genenames.org/cgi-bin/gene\\_symbol\\_report?q=data/hgnc\\_data.php&hgnc\\_id=4877](http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=4877)
- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/8820>
- UniProt  
<http://www.uniprot.org/uniprot/Q9UBX0>

## Sources for This Summary

- Brickman JM, Clements M, Tyrell R, McNay D, Woods K, Warner J, Stewart A, Beddington RS, Dattani M. Molecular effects of novel mutations in HESX1/HESX1 associated with human pituitary disorders. *Development*. 2001 Dec;128(24):5189-99.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/11748154>
- Carvalho LR, Woods KS, Mendonca BB, Marcal N, Zamparini AL, Stifani S, Brickman JM, Arnhold IJ, Dattani MT. A homozygous mutation in HESX1 is associated with evolving hypopituitarism due to impaired repressor-corepressor interaction. *J Clin Invest*. 2003 Oct;112(8):1192-201.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/14561704>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC213489/>
- Dattani MT, Martinez-Barbera JP, Thomas PQ, Brickman JM, Gupta R, Mårtensson IL, Toresson H, Fox M, Wales JK, Hindmarsh PC, Krauss S, Beddington RS, Robinson IC. Mutations in the homeobox gene HESX1/Hesx1 associated with septo-optic dysplasia in human and mouse. *Nat Genet*. 1998 Jun;19(2):125-33.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/9620767>
- Dattani MT, Robinson IC. HESX1 and Septo-Optic Dysplasia. *Rev Endocr Metab Disord*. 2002 Dec;3(4):289-300. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/12424431>
- Kato Y, Kimoto F, Susa T, Nakayama M, Ishikawa A, Kato T. Pituitary homeodomain transcription factors HESX1 and PROP1 form a heterodimer on the inverted TAAT motif. *Mol Cell Endocrinol*. 2010 Feb 5;315(1-2):168-73. doi: 10.1016/j.mce.2009.10.006. Epub 2009 Oct 29.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/19879326>
- McNay DE, Turton JP, Kelberman D, Woods KS, Brauner R, Papadimitriou A, Keller E, Keller A, Haufs N, Krude H, Shalet SM, Dattani MT. HESX1 mutations are an uncommon cause of septooptic dysplasia and hypopituitarism. *J Clin Endocrinol Metab*. 2007 Feb;92(2):691-7. Epub 2006 Dec 5.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17148560>
- Sobrier ML, Maghnie M, Vié-Luton MP, Secco A, di Iorgi N, Lorini R, Amselem S. Novel HESX1 mutations associated with a life-threatening neonatal phenotype, pituitary aplasia, but normally located posterior pituitary and no optic nerve abnormalities. *J Clin Endocrinol Metab*. 2006 Nov;91(11):4528-36. Epub 2006 Aug 29.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16940453>
- Sobrier ML, Netchine I, Heinrichs C, Thibaud N, Vié-Luton MP, Van Vliet G, Amselem S. Alu-element insertion in the homeodomain of HESX1 and aplasia of the anterior pituitary. *Hum Mutat*. 2005 May;25(5):503.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/15841484>
- Tajima T, Hattori T, Nakajima T, Okuhara K, Sato K, Abe S, Nakae J, Fujieda K. Sporadic heterozygous frameshift mutation of HESX1 causing pituitary and optic nerve hypoplasia and combined pituitary hormone deficiency in a Japanese patient. *J Clin Endocrinol Metab*. 2003 Jan;88(1):45-50.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/12519827>
- Thomas PQ, Dattani MT, Brickman JM, McNay D, Warne G, Zacharin M, Cameron F, Hurst J, Woods K, Dunger D, Stanhope R, Forrest S, Robinson IC, Beddington RS. Heterozygous HESX1 mutations associated with isolated congenital pituitary hypoplasia and septo-optic dysplasia. *Hum Mol Genet*. 2001 Jan 1;10(1):39-45.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/11136712>

---

Reprinted from Genetics Home Reference:  
<https://ghr.nlm.nih.gov/gene/HESX1>

Reviewed: March 2010  
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications  
U.S. National Library of Medicine  
National Institutes of Health  
Department of Health & Human Services